

DOCKETED

JAN 24 2007

LOAN RECEIVED

P&T OFFICE ACKNOWLEDGEMENT

ATTORNEY	DATE
Sheldon O. Heber	01/24/07
CASE NUMBER/ 21564YP	SERIAL NUMBER 10/577,893
DATE FILED May 1, 2006	
APPLICANT Ludmerer, Steven W. et al.	
EXPRESS MAIL NO.	

The Patent & Trademark Office acknowledges, and has stamped hereon, the date of the receipt of the items checked below:

- AMENDMENT
- APPEAL AND FEE
- ASSIGNMENT
- BRIEF
- CERTIFICATE OF CORRECTION
- FINAL FEE
- LETTER
- REQUEST FOR F.F. LICENSE
- INFORMATION DISCLOSURE STATEMENT
- PTO 1449 & REFERENCES
- PETITION FOR EXTENSION OF TIME & FEE
- INVITATION TO CORRECT
- DEMAND-CHAPTER II & FEE SHEET
- Sequence Listing w/Disk
- Notice to Comply. . . Seq. Discl.
- Raw Sequence Listing Error Report

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Ludmerer, Steven W. <i>et al.</i>	
Serial No.:	10/577,893	Case No.: 21564YP
Filed:	May 1, 2006	
For:	HCV REPLICONS CONTAINING NS5B FROM GENOTYPE 2B	

Art Unit:

Examiner:

Commission for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RECEIVED

JAN 24 2007

LOAN COPIES ONLY

AMENDMENT

Sir:

Responsive to the Notice to Comply mailed January 5, 2007, applicants request the present application be amended as follows:

Amendments to the Specification begin on page 2 of this paper.

Remarks/Arguments begin on page 3 of this paper.

37 C.F.R. 1.8 Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria VA 22313-1450, on the date appearing below.

MERCK & CO., INC.

By Sheldon O. Heber

Date January 24, 2007

Sheldon O. Heber

Amendments to the Specification:

Please amend the specification by entering the enclosed Sequence Listing.

Remarks/Arguments

Enclosed with the present amendment is a copy of the Notice to Comply, the sequence listing printout accompanying the Notice to Comply, and an amended Sequence Listing provided in hard copy and computer readable form. The amendments to the Sequence Listing update the general information section and correct the description of features indicated in the Notice to Comply for SEQ ID NOs: 1, 24 and 27. The description for SEQ ID NO: 1 was amended to indicate Xaa in position 392, instead of position 376. The description for SEQ ID NO: 24 was amended to provide a correct spelling for "Artificial". The description for SEQ ID NO: 27 was amended to indicate "Artificial".

No new matter is introduced into the Sequence Listing. I hereby state that the contents of the paper and computer readable copies of the enclosed Sequence Listing are the same.

Please charge deposit account 13-2755 for fees due in connection with this amendment. If any time extensions are needed for the timely filing of the present amendment, applicants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By Sheldon O. Heber
Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicant(s)

Merck & Co., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-1958

SEQUENCE LISTING

<110> Ludmerer, Steven W.
Graham, Donald J.
LaFemina, Robert L.
Flores, Osvaldo A.
Pizzuti, Maura
Traboni, Cinzia

<120> HCV REPLICONS CONTAINING NS5B FROM
GENOTYPE 2B

<130> 21564YP

DOCKETED

144 2 A 708

LOSS OF PAPERS

<140> 10/577,893

<141> 2006-05-01

<150> PCT/US2004/036575

<151> 2004-11-03

<150> 60/517,605

<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> VARIANT

<222> (5)...(5)

<223> Xaa = threonine or serine

<221> VARIANT

<222> (24)...(24)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (31)...(31)

<223> Xaa = methionine or isoleucine

<221> VARIANT

<222> (392)...(392)

<223> Xaa = isoleucine or leucine

<400> 1

Ser Met Ser Tyr Xaa Trp Thr Gly Ala Leu Ile Thr Pro Cys Gly Pro
1 5 10 15

Glu	Glu	Glu	Lys	Leu	Pro	Ile	Xaa	Pro	Leu	Ser	Asn	Ser	Leu	Xaa	Arg
				20				25					30		
Phe	His	Asn	Lys	Val	Tyr	Ser	Thr	Thr	Ser	Arg	Ser	Ala	Ser	Leu	Arg
				35				40				45			
Ala	Lys	Lys	Val	Thr	Phe	Asp	Arg	Val	Gln	Val	Leu	Asp	Ala	His	Tyr
				50				55			60				
Asp	Ser	Val	Leu	Gln	Asp	Val	Lys	Arg	Ala	Ala	Ser	Lys	Val	Ser	Ala
				65				70			75		80		
Arg	Leu	Leu	Thr	Val	Glu	Glu	Ala	Cys	Ala	Leu	Thr	Pro	Pro	His	Ser
				85					90			95			
Ala	Lys	Ser	Arg	Tyr	Gly	Phe	Gly	Ala	Lys	Glu	Val	Arg	Ser	Leu	Ser
				100				105			110				
Arg	Arg	Ala	Val	Asn	His	Ile	Arg	Ser	Val	Trp	Glu	Asp	Leu	Leu	Glu
				115				120			125				
Asp	Gln	His	Thr	Pro	Ile	Asp	Thr	Thr	Ile	Met	Ala	Lys	Asn	Glu	Val
				130				135			140				
Phe	Cys	Ile	Asp	Pro	Thr	Lys	Gly	Gly	Lys	Lys	Pro	Ala	Arg	Leu	Ile
				145				150			155		160		
Val	Tyr	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr
				165					170			175			
Asp	Ile	Ala	Gln	Lys	Leu	Pro	Lys	Ala	Ile	Met	Gly	Pro	Ser	Tyr	Gly
				180				185			190				
Phe	Gln	Tyr	Ser	Pro	Ala	Glu	Arg	Val	Asp	Phe	Leu	Leu	Lys	Ala	Trp
				195				200			205				
Gly	Ser	Lys	Lys	Asp	Pro	Met	Gly	Phe	Ser	Tyr	Asp	Thr	Arg	Cys	Phe
				210				215			220				
Asp	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Ser	Ile	Tyr
				225				230			235		240		
Gln	Ala	Cys	Ser	Leu	Pro	Gln	Glu	Ala	Arg	Thr	Val	Ile	His	Ser	Leu
				245					250			255			
Thr	Glu	Arg	Leu	Tyr	Val	Gly	Gly	Pro	Met	Thr	Asn	Ser	Lys	Gly	Gln
				260					265			270			
Ser	Cys	Gly	Tyr	Arg	Arg	Cys	Arg	Ala	Ser	Gly	Val	Phe	Thr	Thr	Ser
				275				280			285				
Met	Gly	Asn	Thr	Met	Thr	Cys	Tyr	Ile	Lys	Ala	Leu	Ala	Ala	Cys	Lys
				290				295			300				
Ala	Ala	Gly	Ile	Val	Asp	Pro	Val	Met	Leu	Val	Cys	Gly	Asp	Asp	Leu
				305				310			315		320		
Val	Val	Ile	Ser	Glu	Ser	Gln	Gly	Asn	Glu	Glu	Asp	Glu	Arg	Asn	Leu
				325					330			335			
Arg	Ala	Phe	Thr	Glu	Ala	Met	Thr	Arg	Tyr	Ser	Ala	Pro	Pro	Gly	Asp
				340				345			350				
Leu	Pro	Arg	Pro	Glu	Tyr	Asp	Leu	Glu	Leu	Ile	Thr	Ser	Cys	Ser	Ser
				355				360			365				
Asn	Val	Ser	Val	Ala	Leu	Asp	Ser	Arg	Gly	Arg	Arg	Arg	Tyr	Phe	Leu
				370				375			380				
Thr	Arg	Asp	Pro	Thr	Thr	Pro	Xaa	Thr	Arg	Ala	Ala	Trp	Glu	Thr	Val
				385				390			395		400		
Arg	His	Ser	Pro	Val	Asn	Ser	Trp	Leu	Gly	Asn	Ile	Ile	Gln	Tyr	Ala
				405					410			415			
Pro	Thr	Ile	Trp	Val	Arg	Met	Val	Ile	Met	Thr	His	Phe	Phe	Ser	Ile
				420					425			430			
Leu	Leu	Ala	Gln	Asp	Thr	Leu	Asn	Gln	Asn	Leu	Asn	Phe	Glu	Met	Tyr
				435				440			445				

Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
 450 455 460
 Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
 465 470 475 480
 Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
 485 490 495
 Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
 500 505 510
 Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
 515 520 525
 Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
 530 535 540
 Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Asp Ile
 545 550 555 560
 Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
 565 570 575
 Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
 580 585 590

<210> 2

<211> 1776

<212> DNA

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> variation

<222> (3)...(3)

<223> n = A or T

<221> variation

<222> (9)...(9)

<223> n = C or A

<221> variation

<222> (13)...(13)

<223> n = A or T

<221> variation

<222> (15)...(15)

<223> n = A or C

<221> variation

<222> (21)...(21)

<223> n = A or G

<221> variation

<222> (24)...(24)

<223> n = C or G

<221> variation

<222> (28)...(28)

<223> n = T or C

```

<221> modified_base
<222> (30)...(30)
<223> n = G or C

<221> variation
<222> (33)...(33)
<223> n = C or A

<221> variation
<222> (71)...(71)
<223> n = A or G

<221> variation
<222> (83)...(83)
<223> n = G or T

<221> variation
<222> (1174)...(1174)
<223> n = A or C

<400> 2
tcnatgtcnt acncntggac nggngccntn atnacaccat gtggggccga agaggagaag 60
ttaccgatca nccctctgag taattcgctc atncggttcc ataataaggt gtactccaca 120
acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacaggggt gcaggtgctg 180
gacgcacact atgactcagt cttgcaggac gttaaagcggg ccgcctctaa ggttagtgcg 240
aggctcctca cggtagagga agcctgcgcg ctgacccgc cccactccgc caaatcgcga 300
tacggatttg gggcaaaaga ggtgcgcagc ttatcttagga gggccgttaa ccacatccgg 360
tccgtgtggg agacactcct ggaagaccaa cataccccaa ttgacacaac tatcatggct 420
aaaaatgagg ttttctgcat tgatccaact aaaggtgggaa aaaagccagc tcgcctcatc 480
gtataccccc accttggggt cagggtgtgc gaaaagatgg ccctctatga catcgaccaa 540
aagttccca aagcgataat ggggccatcc tatgggttcc aatactctcc cgcagaacgg 600
gtcgatttcc tcctcaaagc ttggggaaagt aagaaggacc caatgggtt ctcgtatgac 660
acccgctgtt ttgactcaac cgtcacggag agggacataa gaacagaaga atccatata 720
caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
tacgttaggag gccccatgac aaacagcaaa gggcaatcct gcggctacag gcgttgccgc 840
gcaagcggtg ttttccccac cagcatgggg aataccatga catgttacat caaagccctt 900
gcagcgtgtt aggctgcagg gatcggtggac cctgttatgt tgggtgtgg agacgacctg 960
gtcgcatct cagagagcca aggttaacgag gaggacgagc gaaacctgag agctttcacg 1020
gaggctatga ccaggtattc cccccctccc ggtgaccttc ccagaccgga atatgacttg 1080
gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcgccc 1140
cggtacttcc taaccagaga ccctacoact ccantcaccc gagctgtttg ggaaacagta 1200
agacactccc ctgtcaattt ttggctggc aacatcatcc agtacgcccc cacaatctgg 1260
gtccggatgg tcataatgac tcacttcttc tccatactat tggccagga cactctgaac 1320
caaaatctca attttgagat gtacggggca gtataactcggt tcaatccatt agacctaccg 1380
gccataattt gaaaggctaca tgggcttgaa gcctttcac tgcacacata ctctccccac 1440
gaactctcac gggtggcagc aactctcaga aaacttggag cgcctccct tagagcgtgg 1500
aagagtcggg cgcgtgcgt gagagcttca ctcatgcggc aaggagcgg ggcggccatt 1560
tgtggccgct acctttcaa ctggccgtt gaaacaaaagc tcaaactcac tccattgccc 1620
gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg ggcggccgg ggggacatt 1680
tatcacagcg tgtcgcatgc ccgacccgc ctattactcc tttgcctact cctacttagc 1740
gtaggagtag gcatttttt actccccat cgatga 1776

<210> 3
<211> 1394
<212> PRT

```

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> VARIANT

<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (904)...(904)

<223> Xaa = valine or alanine

<400> 3

Met	Ala	Pro	Ile	Thr	Ala	Tyr	Ser	Gln	Gln	Thr	Arg	Gly	Leu	Leu	Gly
1										10					15
Cys	Ile	Ile	Thr	Ser	Leu	Thr	Gly	Arg	Asp	Lys	Asn	Gln	Val	Glu	Gly
										25					30
Glu	Val	Gln	Val	Val	Ser	Thr	Ala	Thr	Gln	Ser	Phe	Leu	Ala	Thr	Cys
										40					45
Val	Asn	Gly	Val	Cys	Trp	Thr	Val	Tyr	His	Gly	Ala	Gly	Ser	Lys	Thr
										55					60
Leu	Ala	Gly	Pro	Lys	Gly	Pro	Ile	Thr	Gln	Met	Tyr	Thr	Asn	Val	Asp
										70					80
Gln	Asp	Leu	Val	Gly	Trp	Gln	Ala	Pro	Pro	Gly	Ala	Arg	Ser	Leu	Thr
										85					95
Pro	Cys	Thr	Cys	Gly	Ser	Ser	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala
										100					110
Asp	Val	Ile	Pro	Val	Arg	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu	
										115					125
Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu
										130					140
Leu	Cys	Pro	Ser	Gly	His	Ala	Val	Gly	Ile	Phe	Arg	Ala	Ala	Val	Cys
										145					160
Thr	Arg	Gly	Val	Ala	Lys	Ala	Val	Asp	Phe	Val	Pro	Val	Glu	Ser	Met
										165					175
Glu	Thr	Thr	Met	Arg	Ser	Pro	Val	Phe	Thr	Asp	Asn	Ser	Ser	Pro	Pro
										180					190
Ala	Val	Pro	Gln	Thr	Phe	Gln	Val	Ala	His	Leu	His	Ala	Pro	Thr	Gly
										195					205
Ser	Gly	Lys	Ser	Thr	Lys	Val	Pro	Ala	Ala	Tyr	Ala	Ala	Gln	Gly	Tyr
										210					220
Lys	Val	Leu	Val	Leu	Asn	Pro	Ser	Val	Ala	Ala	Thr	Leu	Gly	Phe	Gly
										225					240
Ala	Tyr	Met	Ser	Lys	Ala	His	Gly	Ile	Asp	Pro	Asn	Ile	Arg	Thr	Gly
										245					255
Val	Arg	Thr	Ile	Thr	Thr	Gly	Ala	Pro	Val	Thr	Tyr	Ser	Thr	Tyr	Gly
										260					270
Lys	Phe	Leu	Ala	Asp	Gly	Gly	Cys	Ser	Gly	Gly	Ala	Tyr	Asp	Ile	Ile
										275					285
Ile	Cys	Asp	Glu	Cys	His	Ser	Thr	Asp	Ser	Thr	Thr	Ile	Leu	Gly	Ile
										290					300
Gly	Thr	Val	Leu	Asp	Gln	Ala	Glu	Thr	Ala	Gly	Ala	Arg	Leu	Val	Val
										305					320
										310					

Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
 325 330 335
 Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
 340 345 350
 Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
 355 360 365
 Cys His Ser Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
 370 375 380
 Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
 385 390 395 400
 Ile Pro Thr Ile Gly Asp Val Val Val Ala Thr Asp Ala Leu Met
 405 410 415
 Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
 420 425 430
 Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
 435 440 445
 Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
 450 455 460
 Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly
 465 470 475 480
 Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
 485 490 495
 Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
 500 505 510
 Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
 515 520 525
 His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
 530 535 540
 Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
 545 550 555 560
 Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
 565 570 575
 Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
 580 585 590
 Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
 595 600 605
 Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
 610 615 620
 Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
 625 630 635 640
 Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
 645 650 655
 Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
 660 665 670
 Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
 675 680 685
 His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
 690 695 700
 Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
 705 710 715 720
 Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
 725 730 735
 Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
 740 745 750

Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
 755 760 765
 Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
 770 775 780
 Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
 785 790 795 800
 Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
 805 810 815
 Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
 820 825 830
 Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
 835 840 845
 Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
 850 855 860
 Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
 865 870 875 880
 Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
 885 890 895
 Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu
 900 905 910
 Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
 915 920 925
 Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
 930 935 940
 Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
 945 950 955 960
 Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
 965 970 975
 Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
 980 985 990
 Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
 995 1000 1005
 Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
 1010 1015 1020
 Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
 1025 1030 1035 1040
 Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
 1045 1050 1055
 Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
 1060 1065 1070
 Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
 1075 1080 1085
 Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
 1090 1095 1100
 Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
 1105 1110 1115 1120
 Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro
 1125 1130 1135
 Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
 1140 1145 1150
 Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
 1155 1160 1165
 Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ile Gln Leu Ser Ala Pro
 1170 1175 1180

Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
 1185 1190 1195 1200
 Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Xaa Ile
 1205 1210 1215
 Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp
 1220 1225 1230
 Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
 1235 1240 1245
 Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
 1250 1255 1260
 Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
 1265 1270 1275 1280
 Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
 1285 1290 1295
 Pro Pro Ile Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
 1300 1305 1310
 Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
 1315 1320 1325
 Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
 1330 1335 1340
 Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
 1345 1350 1355 1360
 Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
 1365 1370 1375
 Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
 1380 1385 1390
 Cys Cys

<210> 4
 <211> 4182
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> modified NS3-5A

<221> variation
 <222> (2711)...(2711)
 <223> n = T or C

<221> variation
 <222> (3645)...(3645)
 <223> n = A or G

<400> 4
 atggcgccca tcacggctta ctcccaaacag acgcggggcc tacttggttg catcatcact 60
 agccttacag gccgggacaa gaaccagggtc gagggagagg ttccagggttgt ttccaccgca 120
 acacaatcct tcctggcgac ctgcgtcaac ggctgtgtt ggaccgttta ccatgggtct 180
 ggctcaaaga ccttagccgg ccoaaagggg ccaatcaccc agatgtacac taatgtggac 240
 caggacctcg tcggctggca ggcccccggggcggtt cttgacacc atgcacccgt 300
 ggcagctcag acctttactt ggtcacgaga catgctgacg tcattccgggt ggcggccgg 360
 ggcgacagta gggggagcct gctctcccc aggcctgtct cctacttgaa gggctttcg 420
 ggtggtccac tgctctgccc ttccgggcac gctgtgggca tcttccgggc tgccgtatgc 480
 acccgggggg ttgcgaaggc ggtggacttt gtgccgttag agtccatgga aactactatg 540

cggtctccgg tcttcacgga caactcatcc ccccccggccg taccgcagac atttcaagtg 600
 gcccacccac acgctcccac tggcagcggc aagagtacta aagtgccggc tgcataatgca 660
 gccaagggt acaagggtgt cgtccctcaat ccgtccgttg ccgctacccctt agggtttggg 720
 gcttatatgt ctaaggcaca cggtatttgc cccaacatca gaactgggggt aaggaccatt 780
 accacaggcg ccccccgtcac atactctacc tatggcaagt ttcttgcga tgggggttgc 840
 tctggggggc cttatgacat cataatatgt gatgagtgcc attcaactga ctcgactaca 900
 atcttgggca tcggcacagt cctggaccaa gcggagacgg ctggagcgcg gcttgcgtg 960
 ctcgcccaccc ctacgcctcc gggatcggtc accgtgccac accccaaacat cgaggaggtg 1020
 gcccgtcta atactggaga gatccccctt tatggcaaaag ccattccccat tgaagccatc 1080
 agggggggaa ggcatctcat tttctgtcat tccaagaaga agtgcgacga gctgcggca 1140
 aagctgtcag gcctcggaat caacgctgtg gcgttattacc gggggctcga tgtgtccgtc 1200
 ataccaacta tcggagacgt cgttgcgtg gcaacagacg ctctgatgac gggctatacg 1260
 ggcgactttg actcagtgtat cgactgttaac acatgtgtca cccagacagt cgacttcagc 1320
 ttggatccca ctttcaccat ttagacgacg accgtgcctc aagacgcagt gtcgcgtc 1380
 cagcggcggg gtaggactgg cagaggttagg atggcatct acagggttgc gactccggg 1440
 gaacggccct cgggcatttt cgattcctcg gtcctgttg agtgcatacg cgccggctgt 1500
 gcttggtacg agtcaccccc cggcgagacc tcgggttagt tgcgggccta cctgaacaca 1560
 ccagggttgc ccgtttgcca ggaccacctg gagttctggg agagtgttctt cacaggcctc 1620
 acccacatag atgcacacatt cttgtccca accaagcagg caggagacaa cttcccctac 1680
 ctggtagcat accaagccac ggtgtgcgc accggctcagg ccccacctcc atcatggat 1740
 caaatgttga agtgcatacg acggctgaaa cctacgctgc acggggcaac acccttgctg 1800
 tacaggctgg gagccgtcca aaatgaggc accctcaccc accccataac caaatacatc 1860
 atggcatgca tgcggctga cttggaggc gtcactagca cctgggtgtc ggtggggcgg 1920
 gtccttgcag ctctggccgc gtattgcctg acaacaggc gtgtggcat tttgggttagg 1980
 attatcttgt ccggggaggcc ggctattgtt cccgacagg agtttctcta ccaggagttc 2040
 gatgaaatgg aagagtgcgc ctcgcacccctc ctttacatcg acggggaaat gcagctcgcc 2100
 gagcaattca agcagaaagc gctcgggtt caagtgccg gccccttgaga cattctggc gaagcacatg 2220
 gctgctcccg tgggggggtc caagtggcg gccccttgaga aactctgtcc tggaaacccc 2280
 tggaaatttca tcagcgggat acagtactt gcaggcttat ccactctgtcc tggaaacccc 2340
 gcaatagcat cattgtatggc attcacagcc tctatcacca gcccgtcac cacccaaagt 2400
 accctctgt ttaacatctt ggggggggtgg gtggctgccc aactcgcccc cccagcgcc 2460
 gcttcggcctt tgcggccgc cggcatcgcc ggtgcggctg ttggcagcat aggcttggg 2520
 aaggtgcttg tggacattct ggcgggttat ggagcaggag tggccggcgc gctcggtggc 2580
 ttcaaggtca tggcggcga gatgccctcc accgaggacc tggtaatct acttctgtcc 2640
 atccctcttc ctggcgccct ggtcgctggg gtcgtgtgtc cagcaatact gcgtcgacac 2700
 gtgggtccgg gagagggggc tggcagatgg atgaaccggc tgatagcggtt cgcctcgccg 2760
 ggttaatcatg ttcccccac gcaatgttg cctgagagcg acgcccgcg ggtgtttact 2820
 cagatcctct ccagccttac catcactcag ctgctgaaaa ggctccacca gtggattaat 2880
 gaagactgtt ccacaccgtt ttccggctcg tggtaaggg atgtttgggat gtcgtatgc 2940
 acgggtttga ctgacttcaa gacctggctc cagtcacatcg tcctgcgcgca gtcaccggg 3000
 gtcctttttt ttcgtgcca acgcgggtac aagggagtct ggcggggaga cggcatcatg 3060
 caaaccaccc gcccattgtgg agcacaatgc accggacatg tcaaaaacgg ttccatgagg 3120
 atcgctgggc ctaagacccatc cagcaacacg tggcatggaa cattccccat caacgcatac 3180
 gcccgttggg aggatgttgc ggtcacgcgg gtgggggatt tccactacgt gacgggcattg 3240
 accactgaca acgtaaatgt cccatgccag gttccggctc ctgaattctt cacggaggtg 3300
 gacggagttgc ggttgacacag gtacgctccg gcgtgcaggc ctctcctacg ggaggaggtt 3360
 acattccagg tcgggtccaa ccaataccatcg tttgggtcac agtaccatg cgagcccgaa 3420
 ccggatgttag cagtgctcac ttccatgtcc accgaccctt cccacatcac agcagaaacg 3480
 gctaagcgta ggttggccag ggggtctccc ccctccttgg ccagctttc agctatccag 3540
 ttgtctgcgc cttcccttgc ggcgacatgc actaccacc atgtctctcc ggacgctgac 3600
 ctcatcgagg ccaacccctt gtggcgccag gagatggcg ggcacatcac cgcgtggag 3660
 tcggagaaca aggtggtagt cctggactct ttcgacccgc ttcgagcgggaa ggaggatgag 3720
 agggaaatgtt ccgttccggc ggagatcctg cggaaatcca agaagttccc cgcaagcgatg 3780
 cccatctggg cgcccccggaa ttacaaccct ccactgttag agtcctggaa ggaccggac 3840

tacgtccctc cggtggtgca cgggtgcccgttgccaccta tcaaggcccc tccaaatacca 3900
 cctccacgga gaaagaggac ggttgcctta acagagtcct ccgtgtcttc tgccttagcg 3960
 gagctcgcta ctaagacctt cggcagctcc gaatcatcg ccgtcgacag cggcacggcg 4020
 accggcccttc ctgaccaggc ctccgacgac ggtgacaaag gatccgacgt tgagtctgtac 4080
 tcctccatgc ccccccgtga gggggaaaccg gggggaccccg atctcaagtga cgggtcttgg 4140
 tctaccgtga gcgaggaagc tagtgaggat gtcgtctgtc gc 4182

<210> 5
 <211> 34
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 5
 aaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaaaa aaaa 34

<210> 6
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 6
 atggagaaga aggtcattgt gtg 23

<210> 7
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 7
 gctcccatta ctgcctacac tca 23

<210> 8
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 8
 ccgctctacc gagcggggag t 21

<210> 9
 <211> 25
 <212> DNA
 <213> Artificial Sequence

<220>	
<223> primer	
<400> 9	
ctctcctcaa gcgtattcaa caagg	25
<210> 10	
<211> 25	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 10	
ccgtgcagcg taggtttcag ccgta	25
<210> 11	
<211> 24	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 11	
cccatatttat gggatctgat ctgg	24
<210> 12	
<211> 28	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 12	
caagctgaag tcgactgtct gggtgaca	28
<210> 13	
<211> 29	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 13	
tacttggtca cgagacatgc tgacgtcat	29
<210> 14	
<211> 19	
<212> DNA	
<213> Artificial Sequence	

<220>		
<223> primer		
<400> 14		
ggagaggata gcagggagt		19
<210> 15		
<211> 29		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> primer		
<400> 15		
cgtatatgtc taaggcacac ggtattgac		29
<210> 16		
<211> 28		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> primer		
<400> 16		
ggctggtgat agaggctgtg aatgccat		28
<210> 17		
<211> 28		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> primer		
<400> 17		
ggatcaaatg tggaaagtgtc tcatacgg		28
<210> 18		
<211> 19		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> primer		
<400> 18		
tcgagggttgt ggagtacac		19
<210> 19		
<211> 29		
<212> DNA		
<213> Artificial Sequence		

<220>	
<223> primer	
<400> 19	
gcaatagcat cattgatggc attcacagc	29
<210> 20	
<211> 20	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 20	
ggcctcgatg aggtcagcgt	20
<210> 21	
<211> 25	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 21	
ctctcctcaa gogtattcaa caagg	25
<210> 22	
<211> 20	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 22	
gtaaaagtgcc cgtgtcaggt	20
<210> 23	
<211> 21	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> primer	
<400> 23	
catgatagtt gtgtcaattg g	21
<210> 24	
<211> 19	
<212> DNA	
<213> Artificial Sequence	

```

<220>
<223> primer

<400> 24
gtctaccgtg agcgagggaa 19

<210> 25
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 25
atactcctgg acagggggccc t 21

<210> 26
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 26
gcgcgcgcat cgatcgaaaa gtaaaaaagat gcctac 36

<210> 27
<211> 783
<212> DNA
<213> Artificial Sequence

<220>
<223> modified NS4B

<400> 27
gcctccaaag ccgcctcat tgaggaaggc cagcgatgg cggagatgct caaatctaag 60
atacaaggcc tcctacaaca ggccacaagg caagctcaag acatacagcc agctatacag 120
tcatcatggc ccaagcttga acaattttgg gccaaacaca tgtggactt catcagtgg 180
atacagtacc tagcaggact ctccacccta ccggaaaatc ctgcagtagc atcaatgtg 240
gcttttagcg cccgcgtgac tagccacta cccaccagca ccaccatcct cttgaacatc 300
atgggaggat ggttggctc tcagattgcc cccccctggc gagccactgg cttcggtgtc 360
agtggcttag tggggggggc cgtcggaaagc ataggcctgg gtaagatact ggtggacgtt 420
ttggccgggt acggcgagg catttcaggc gcccctgttag cttttaagat catgagcggc 480
gagaagccca cggtagaaga cgttgtgaat ctccctgcctg ctattctgtc tcctgggtgc 540
ttggtagtgg gagtcatctg tgcagcaatc ctgcgtcgac acgtgggtcc gggagaggg 600
gctgtgcagt ggtatgaaaccg gctgatagcg ttccgcctcgcc gggtaatca tgcttcccc 660
acgcactatg tgcctgagag cgacgcgcga ggcgcgtgtta ctcagatcct ctccagcctt 720
accatcaactc agctgctgaa aaggctccac cagtggatta atgaagactg ctccacacccg 780
tgt 783

<210> 28
<211> 261

```

<212> PRT
<213> Artificial Sequence

<220>
<223> modified NS4B

<400> 28
Ala Ser Lys Ala Ala Leu Ile Glu Glu Gly Gln Arg Met Ala Glu Met
1 5 10 15
Leu Lys Ser Lys Ile Gln Gly Leu Leu Gln Gln Ala Thr Arg Gln Ala
20 25 30
Gln Asp Ile Gln Pro Ala Ile Gln Ser Ser Trp Pro Lys Leu Glu Gln
35 40 45
Phe Trp Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu
50 55 60
Ala Gly Leu Ser Thr Leu Pro Gly Asn Pro Ala Val Ala Ser Met Met
65 70 75 80
Ala Phe Ser Ala Ala Leu Thr Ser Pro Leu Pro Thr Ser Thr Thr Ile
85 90 95
Leu Leu Asn Ile Met Gly Gly Trp Leu Ala Ser Gln Ile Ala Pro Pro
100 105 110
Ala Gly Ala Thr Gly Phe Val Val Ser Gly Leu Val Gly Ala Ala Val
115 120 125
Gly Ser Ile Gly Leu Gly Lys Ile Leu Val Asp Val Leu Ala Gly Tyr
130 135 140
Gly Ala Gly Ile Ser Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly
145 150 155 160
Glu Lys Pro Thr Val Glu Asp Val Val Asn Leu Leu Pro Ala Ile Leu
165 170 175
Ser Pro Gly Ala Leu Val Val Gly Val Ile Cys Ala Ala Ile Leu Arg
180 185 190
Arg His Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu
195 200 205
Ile Ala Phe Ala Ser Arg Gly Asn His Ala Ser Pro Thr His Tyr Val
210 215 220
Pro Glu Ser Asp Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu
225 230 235 240
Thr Ile Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp
245 250 255
Cys Ser Thr Pro Cys
260

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

DEBORAH D WILLIAMS

Telephone: (703) 308-9140 EXT 205

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/577,893	PCT/US04/36575	21564Y

FORM PCT/DO/EO/922 (371 Formalities Notice)

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/577,893
Source: JFLWP
Date Processed by STIC: 05/11/2006

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
- 2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.4.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail. Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom. Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

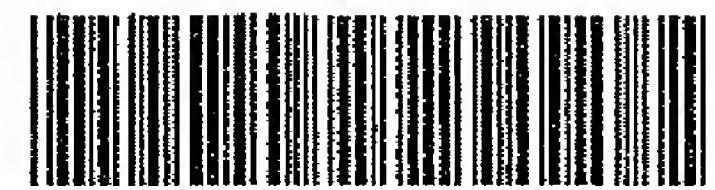
1. **EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)**
2. **U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05): U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314**

Revised 01/10/06

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

By Shelley Date 1-24-07



IFWP

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

4 <110> APPLICANT: Merck & Co., Inc.
5 Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.
7 <120> TITLE OF INVENTION: HCV REPLICONS CONTAINING NS5B FROM
8 GENOTYPE 2B
10 <130> FILE REFERENCE: 21564Y PCT
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/577,893
C--> 12 <141> CURRENT FILING DATE: 2006-05-01
12 <150> PRIOR APPLICATION NUMBER: 60/517,605
13 <151> PRIOR FILING DATE: 2003-11-05
15 <160> NUMBER OF SEQ ID NOS: 28
17 <170> SOFTWARE: FastSEQ for Windows Version 4.0
19 <210> SEQ ID NO: 1
20 <211> LENGTH: 591
21 <212> TYPE: PRT
22 <213> ORGANISM: Artificial Sequence
24 <220> FEATURE:
25 <223> OTHER INFORMATION: modified NS5B
W--> 27 <221> NAME/KEY: VARIANT
28 <222> LOCATION: (5) ... (5)
29 <223> OTHER INFORMATION: Xaa = threonine or serine
W--> 31 <221> VARIANT
32 <222> LOCATION: (24) ... (24)
33 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 35 <221> VARIANT
36 <222> LOCATION: (31) ... (31)
37 <223> OTHER INFORMATION: Xaa = methionine or isoleucine
W--> 39 <221> VARIANT
40 <222> LOCATION: (376) ... (376) *at this location* Set
41 <223> OTHER INFORMATION: Xaa = isoleucine or leucine *at this location*
W--> 43 <400> 1
W--> 44 Ser Met Ser Tyr Xaa Trp Thr Gly Ala Leu Ile Thr Pro Cys Gly Pro
45 1 5 10 15
W--> 46 Glu Glu Glu Lys Leu Pro Ile Xaa Pro Leu Ser Asn Ser Leu Xaa Arg
47 20 25 30
48 Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
49 35 40 45
50 Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
51 50 55 60
52 Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
53 65 70 75 80
54 Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
55 85 90 95
56 Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser

392

RAW SEQUENCE LISTING DATE: 05/11/2006
 PATENT APPLICATION: US/10/577,893 TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
 Output Set: N:\CRF4\05112006\J577893.raw

57	100	105	110
58	Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu		
59	115	120	125
60	Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val		
61	130	135	140
62	Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile		
63	145	150	155
64	160	Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr	
65	165	170	175
66	Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly		
67	180	185	190
68	Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp		
69	195	200	205
70	Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe		
71	210	215	220
72	Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr		
73	225	230	235
74	240	Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu	
75	245	250	255
76	260	265	270
77	275	280	285
78	Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser		
79	290	295	300
80	305	310	315
81	320	325	330
82	335	Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu	
83	340	345	350
84	355	360	365
85	370	375	380
86	Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Tyr Phe Leu		
87	385	390	395
88	400	Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala	
89	405	410	415
90	420	425	430
91	430	435	440
92	440	Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr	
93	445	450	455
94	460	Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu	
95	465	470	475
96	480	Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His	
97	485	490	495
98	Glü Leü Ser Arg Val Ala Ala Thr Leu Arg Lys Leü Gly Ala Pro Pro		
99	100		
100			
101			
102			
103			
104			
105			

? X99

RAW SEQUENCE LISTING DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893 TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

106 Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
107 500 505 510
108 Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
109 515 520 525
110 Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
111 530 535 540
112 Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Asp Ile
113 545 550 555 560
114 Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Cys Leu
115 565 570 575
116 Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
117 580 585 590
120 <210> SEQ ID NO: 2
121 <211> LENGTH: 1776
122 <212> TYPE: DNA
123 <213> ORGANISM: Artificial Sequence
125 <220> FEATURE:
126 <223> OTHER INFORMATION: modified NS5B
W--> 128 <221> NAME/KEY: variation
129 <222> LOCATION: (3)...(3)
130 <223> OTHER INFORMATION: n = A or T
W--> 132 <221> variation
133 <222> LOCATION: (9)...(9)
134 <223> OTHER INFORMATION: n = C or A
W--> 136 <221> variation
137 <222> LOCATION: (13)...(13)
138 <223> OTHER INFORMATION: n = A or T
W--> 140 <221> variation
141 <222> LOCATION: (15)...(15)
142 <223> OTHER INFORMATION: n = A or C
W--> 144 <221> variation
145 <222> LOCATION: (21)...(21)
146 <223> OTHER INFORMATION: n = A or G
W--> 148 <221> variation
149 <222> LOCATION: (24)...(24)
150 <223> OTHER INFORMATION: n = C or G
W--> 152 <221> variation
153 <222> LOCATION: (28)...(28)
154 <223> OTHER INFORMATION: n = T or C
W--> 156 <221> modified_base
157 <222> LOCATION: (30)...(30)
158 <223> OTHER INFORMATION: n = G or C
W--> 160 <221> variation
161 <222> LOCATION: (33)...(33)
162 <223> OTHER INFORMATION: n = C or A
W--> 164 <221> variation
165 <222> LOCATION: (71)...(71)
166 <223> OTHER INFORMATION: n = A or G
W--> 168 <221> variation

RAW SEQUENCE LISTING DATE: 05/11/2006
 PATENT APPLICATION: US/10/577,893 TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
 Output Set: N:\CRF4\05112006\J577893.raw

169 <222> LOCATION: (83) . . . (83)
 170 <223> OTHER INFORMATION: n = G or T
 W--> 172 <221> variation
 173 <222> LOCATION: (1174) . . . (1174)
 174 <223> OTHER INFORMATION: n = A or C
 W--> 176 <400> 2
 W--> 177 tcnatgtcnt acncntggac nggngccntn atnacaccat gtggggcccga agaggagaag 60
 W--> 178 ttacccatca nccctctgag taattcgctc atncggttcc ataataaggt gtactccaca 120
 179 acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
 180 gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
 181 aggctctca cggtagagga agcctgcgcg ctgacccgc cccactccgc caaatcgcga 300
 182 tacggatttg gggcaaaaaga ggtgcgcagc ttatcttagga gggccgttaa ccacatccgg 360
 183 tccgtgtggg aggacccctt ggaagacccaa cataccccaa ttgacacacaac tatcatggct 420
 184 aaaaatgagg tggctctgcattt gatccaaact aaaggtggga aaaagccagc tcgcctcatc 480
 185 gtatacccg accttgggtt caggggtgtgc gaaaagatgg ccctctatga catcgcacaa 540
 186 aagcttccca aagcgataat gggccatcc tatgggttcc aatactctcc cgcagaacgg 600
 187 gtcgatttcc tcctcaaaggc ttggggaaatg aagaaggacc caatgggtt ctcgtatgac 660
 188 acccgctgtt ttgactcaac cgtcacggag agggacataa gaacagaaga atccatata 720
 189 caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
 190 tacgttaggag ggcgcattgac aaacagccaa gggcaatccct gggctacag gcgttgcgc 840
 191 gcaaggcgtg ttttaccac cagcatgggg aataccatga catgttacat caaagccctt 900
 192 gcagcgtgtttaaaggctcagg gatcggtggac cctgttatgt tgggtgtgg agacgacctg 960
 193 gtcgtcatct cagagagccaa aggttaacgag gaggacggc gaaacctgag agctttcacg 1020
 194 gaggctatga ccaggtattt cgcgcctccc ggtgacccctt ccagaccggaa atatgacttg 1080
 195 gagcttataa catcctgctc ctcaaaacgta tcggtagcgc tggactctcg gggtcgcgc 1140
 W--> 196 cggtaatcc taaccagaga ccctaccact ccantccacc gagctgtttt gggaaacagta 1200
 197 agacactccc ctgtcaattt ttggctgggc aacatcatcc agtacgcccc cacaatctgg 1260
 198 gtccggatgg tcataatgac tcacttcttc tccataactat tggcccgagg cactctgaac 1320
 199 caaaaatctca atttttagat gtacggggca gtatactgg tcaatccatt agacccatcg 1380
 200 gccataattt aaaggctaca tgggcttgaa gcctttcac tgcacacata ctctccccc 1440
 201 gaactctcac ggggtggcagc aactctcaga aaacttggag cgcctccct tagagcgtgg 1500
 202 aagagtccggc cgcgtgccgt gagagcttca ctcatcgccc aaggagccgag ggcggccatt 1560
 203 tgtggccgct acctcttcaa ctggggcggtg aaaacaaaagc tcaaactcac tccattgcc 1620
 204 gaggcgagcc gcctggattt atccgggtgg ttcacccgtgg ggcgcggcgg gggcgacatt 1680
 205 tatcacagcg tgcgcattgc ccgaccccgcc tattactcc tttgcctact cctacttagc 1740
 206 gtaggatgt gcatctttt actcccccgt cgtatca 1776
 208 <210> SEQ ID NO: 3
 209 <211> LENGTH: 1394
 210 <212> TYPE: PRT
 211 <213> ORGANISM: Artificial Sequence
 213 <220> FEATURE:
 214 <223> OTHER INFORMATION: modified NS3-5A
 W--> 216 <221> NAME/KEY: VARIANT
 217 <222> LOCATION: (1215) . . . (1215)
 218 <223> OTHER INFORMATION: Xaa = asparagine or serine
 W--> 220 <221> VARIANT
 221 <222> LOCATION: (904) . . . (904)
 222 <223> OTHER INFORMATION: Xaa = valine or alanine
 W--> 224 <400> 3

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

225 Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
226 1 5 10 15
227 Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
228 20 25 30
229 Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
230 35 40 45
231 Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
232 50 55 60
233 Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
234 65 70 75 80
235 Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
236 85 90 95
237 Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
238 100 105 110
239 Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
240 115 120 125
241 Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
242 130 135 140
243 Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
244 145 150 155 160
245 Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
246 165 170 175
247 Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
248 180 185 190
249 Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
250 195 200 205
251 Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
252 210 215 220
253 Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
254 225 230 235 240
255 Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
256 245 250 255
257 Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
258 260 265 270
259 Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
260 275 280 285
261 Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
262 290 295 300
263 Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
264 305 310 315 320
265 Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
266 325 330 335
267 Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
268 340 345 350
269 Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
270 355 360 365
271 Cys His Ser Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
272 370 375 380
273 Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val

10/577,893

6

<210> 24

<211> 19

<212> DNA

<213> Artificial Sequence

<400> 24

gtctaccgtg agcgagggaa

If <213> Responses are
Artificial or Unknown.

Pls Explain the Source
of genetic Material.
See Item 11 on Error
Summary Sheet.

10/577,893

7

<210> 27

<211> 783

<212> DNA

<213> modified NS4B

<400> 27

22137 Responses can only
be Artificial, Unknown
or Genus Species. See
Item 10 on Error Summary
Sheet.

RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 5,24,31,392
Seq#:2; N Pos. 3,9,13,15,21,24,28,30,33,71,93,1174
Seq#:3; Xaa Pos. 904,1215
Seq#:4; N Pos. 3644

Use of <220> Feature(NEW RULES):

Sequence(s) are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence"
or "Unknown". Please explain source of genetic material in <220> to <223>
section (See "Federal Register," 6/01/98, Vol. 63, No. 104, pp.29631-32)
(Sec.1.823 of new Rules)

Seq#:1,2,3,4,24

VERIFICATION SUMMARY DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893 TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

L:12 M:270 C: Current Application Number differs, Replaced Current Application No
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:27 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:31 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:35 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:39 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:43 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:44 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:46 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:16
L:92 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:384
L:128 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:132 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:136 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:140 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:144 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:148 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:152 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:156 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:160 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:164 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:168 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:172 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:176 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:177 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:178 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:60
L:196 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:1140
L:216 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:220 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:224 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:337 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:896
L:375 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:1200
L:411 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:415 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:419 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:480 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:3600
L:703 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:24
L:705 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:24, Line#:705

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/577,893
Source: TFW/P
Date Processed by STIC: 05/11/2006

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.4.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

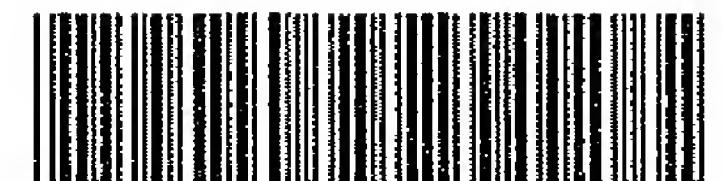
Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

- 1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>), EFS Submission User Manual - ePAVE)**
- 2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**
- 3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05): U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314**

Revised 01/10/06



RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

4 <110> APPLICANT: Merck & Co., Inc.
5 Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.
7 <120> TITLE OF INVENTION: HCV REPLICONS CONTAINING NS5B FROM
8 GENOTYPE 2B
10 <130> FILE REFERENCE: 21564Y PCT
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/577,893
C--> 12 <141> CURRENT FILING DATE: 2006-05-01
12 <150> PRIOR APPLICATION NUMBER: 60/517,605
13 <151> PRIOR FILING DATE: 2003-11-05
15 <160> NUMBER OF SEQ ID NOS: 28
17 <170> SOFTWARE: FastSEQ for Windows Version 4.0
19 <210> SEQ ID NO: 1
20 <211> LENGTH: 591
21 <212> TYPE: PRT
22 <213> ORGANISM: Artificial Sequence
24 <220> FEATURE:
25 <223> OTHER INFORMATION: modified NS5B
W--> 27 <221> NAME/KEY: VARIANT
28 <222> LOCATION: (5)...(5)
29 <223> OTHER INFORMATION: Xaa = threonine or serine
W--> 31 <221> VARIANT
32 <222> LOCATION: (24)...(24)
33 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 35 <221> VARIANT
36 <222> LOCATION: (31)...(31)
37 <223> OTHER INFORMATION: Xaa = methionine or isoleucine
W--> 39 <221> VARIANT
40 <222> LOCATION: (376)...(376) *at this location* → *Set*
41 <223> OTHER INFORMATION: Xaa = isoleucine or leucine *at this location*
W--> 43 <400> 1
W--> 44 Ser Met Ser Tyr Xaa Trp Thr Gly Ala Leu Ile Thr Pro Cys Gly Pro
45 1 5 10 15
W--> 46 Glu Glu Glu Lys Leu Pro Ile Xaa Pro Leu Ser Asn Ser Leu Xaa Arg
47 20 25 30
48 Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
49 35 40 45
50 Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
51 50 55 60
52 Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
53 65 70 75 80
54 Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
55 85 90 95
56 Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser

*Does Not Comply
Corrected Diskette Needed
(pg 1,2,6,7)*

at this location → *Set*
at this location → *Set*
392

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

57	100	105	110
58	Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu		
59	115	120	125
60	Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val		
61	130	135	140
62	Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Pro Ala Arg Leu Ile		
63	145	150	155
64	160		
65	Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr		
66	165	170	175
67	Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly		
68	180	185	190
69	Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp		
70	195	200	205
71	Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe		
72	210	215	220
73	Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr		
74	225	230	235
75	240		
76	Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu		
77	245	250	255
78	Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln		
79	260	265	270
80	Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser		
81	275	280	285
82	Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys		
83	290	295	300
84	82 Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu		
85	305	310	315
86	320		
87	Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu		
88	325	330	335
89	Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp		
90	340	345	350
91	Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser		
92	355	360	365
93	90 Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Tyr Phe Leu		
94	370	375	380
95	W--> Thr Arg Asp Pro Thr Thr Pro Xaa Thr Arg Ala Ala Trp Glu Thr Val		
96	385	390	395
97	400		
98	Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala		
99	405	410	415
100	Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile		
101	420	425	430
102	Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr		
103	435	440	445
104	Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu		
105	450	455	460
	Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His		
	465	470	475
	480		
	Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro		
	485	490	495

→? X93

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

106 Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
107 500 505 510
108 Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
109 515 520 525
110 Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
111 530 535 540
112 Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Asp Ile
113 545 550 555 560
114 Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Cys Leu
115 565 570 575
116 Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
117 580 585 590
120 <210> SEQ ID NO: 2
121 <211> LENGTH: 1776
122 <212> TYPE: DNA
123 <213> ORGANISM: Artificial Sequence
125 <220> FEATURE:
126 <223> OTHER INFORMATION: modified NS5B
W--> 128 <221> NAME/KEY: variation
129 <222> LOCATION: (3)...(3)
130 <223> OTHER INFORMATION: n = A or T
W--> 132 <221> variation
133 <222> LOCATION: (9)...(9)
134 <223> OTHER INFORMATION: n = C or A
W--> 136 <221> variation
137 <222> LOCATION: (13)...(13)
138 <223> OTHER INFORMATION: n = A or T
W--> 140 <221> variation
141 <222> LOCATION: (15)...(15)
142 <223> OTHER INFORMATION: n = A or C
W--> 144 <221> variation
145 <222> LOCATION: (21)...(21)
146 <223> OTHER INFORMATION: n = A or G
W--> 148 <221> variation
149 <222> LOCATION: (24)...(24)
150 <223> OTHER INFORMATION: n = C or G
W--> 152 <221> variation
153 <222> LOCATION: (28)...(28)
154 <223> OTHER INFORMATION: n = T or C
W--> 156 <221> modified_base
157 <222> LOCATION: (30)...(30)
158 <223> OTHER INFORMATION: n = G or C
W--> 160 <221> variation
161 <222> LOCATION: (33)...(33)
162 <223> OTHER INFORMATION: n = C or A
W--> 164 <221> variation
165 <222> LOCATION: (71)...(71)
166 <223> OTHER INFORMATION: n = A or G
W--> 168 <221> variation

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

169 <222> LOCATION: (83) ... (83)
170 <223> OTHER INFORMATION: n = G or T
W--> 172 <221> variation
173 <222> LOCATION: (1174) ... (1174)
174 <223> OTHER INFORMATION: n = A or C
W--> 176 <400> 2
W--> 177 tcnatgtcnt acnentggac nggngccntn atnacaccat gtggggccga agaggagaag 60
W--> 178 ttacccatca nccctctgag taattcgtctc atnccgttcc ataataaggt gtactccaca 120
179 acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacaggggt gcagggctg 180
180 gacgcacact atgactcagt cttgcaggac gttaaagcggg cccactccgc cccactccgc 240
181 aggctcctca cggtagagga agcctgcgcg ctgaccggc cccactccgc cccactccgc 300
182 tacggatgg gggcaaaaga ggtgcgcagc ttatcttagga gggccgttaa ccacatccgg 360
183 tccgtgtgg aggacccctt ggaagaccaa catacccaa ttgacacacaac tatcatggct 420
184 aaaaatgagg tggctctgcat tgatccaaact aaaggtgggaa aaaagccagc tcgcctcatc 480
185 gtataccccc accttggggt cagggtgtgc gaaaagatgg ccctctatga catcgaccaa 540
186 aagcttccca aagcgataat gggccatcc tatgggttcc aataactctcc cgcagaacgg 600
187 gtcgatttcc tcctcaaagg ttggggaaat aagaaggacc caatgggtt ctcgtatgac 660
188 acccgctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
189 caggcttggc ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
190 tacgttaggag gggccatgac aaaaacagcaaa gggcaatccct gcccgtacag gcccgtccgc 840
191 gcaagcggtg ttttccccac cagcatgggg aataccatga catgttacat caaagccctt 900
192 gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tgggtgtgtgg agaogacctg 960
193 gtcgtcatct cagagagcca aggttaacgag gaggacgagc gaaacctgag agctttcacg 1020
194 gaggctatga ccaggtattc cggccctccc ggtgaccttc ccagaccgga atatgactt 1080
195 gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcggc 1140
W--> 196 cggtaacttcc taaccagaga cccttaccact ccantcaccc gagctgtttg ggaaacagta 1200
197 agacactccc ctgtcaattt ttggctggc aacatcatcc agtacgcccc cacaatctgg 1260
198 gtccggatgg tcataatgac tcacttcttcc tccataactat tggcccgaga cactctgaac 1320
199 caaaatctca atttttagat gtacggggca gtataactcgg tcaatccatt agacccatcg 1380
200 gccataattt aaaggctaca tgggttttgc gcttttcac tgcacacata ctctcccccac 1440
201 gaactctcac ggggtggcagc aactctcaga aaacttggag cgcctccct tagagcgtgg 1500
202 aagagtccgg cgcgtggcgt gagagcttca ctcatcgccc aaggagcgg ggcggccatt 1560
203 tgtggccgct acctcttcaa ctggggcggtg aaaacaaaagc tcaaactcac tccattgccc 1620
204 gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg ggcggccgg gggcgacatt 1680
205 tatcacagcg tgcgtcatgc cccacccgc ctattactcc tttgcctact cctacttagc 1740
206 gtaggagtag gcatctttt actcccccgtat cgatga 1776
208 <210> SEQ ID NO: 3
209 <211> LENGTH: 1394
210 <212> TYPE: PRT
211 <213> ORGANISM: Artificial Sequence
213 <220> FEATURE:
214 <223> OTHER INFORMATION: modified NS3-5A
W--> 216 <221> NAME/KEY: VARIANT
217 <222> LOCATION: (1215) ... (1215)
218 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 220 <221> VARIANT
221 <222> LOCATION: (904) ... (904)
222 <223> OTHER INFORMATION: Xaa = valine or alanine
W--> 224 <400> 3

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893DATE: 05/11/2006
TIME: 11:07:16Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

225 Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
226 1 5 10 15
227 Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
228 20 25 30
229 Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
230 35 40 45
231 Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
232 50 55 60
233 Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
234 65 70 75 80
235 Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
236 85 90 95
237 Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
238 100 105 110
239 Asp Val Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
240 115 120 125
241 Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
242 130 135 140
243 Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
244 145 150 155 160
245 Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
246 165 170 175
247 Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
248 180 185 190
249 Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
250 195 200 205
251 Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
252 210 215 220
253 Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
254 225 230 235 240
255 Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
256 245 250 255
257 Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
258 260 265 270
259 Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
260 275 280 285
261 Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
262 290 295 300
263 Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
264 305 310 315 320
265 Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
266 325 330 335
267 Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
268 340 345 350
269 Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
270 355 360 365
271 Cys His Ser Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
272 370 375 380
273 Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val

9/577,893

6

<210> 24

<211> 19

<212> DNA

<213> Artificial Sequence

<400> 24

gtctaccgtg agcgagga

If <213> Responses are
Artificial or Unknown.

Pls Explains the Source
of genetic Material.
See Item 11 on Error
Summary Sheet.

0/577,893

7

<210> 27

<211> 783

<212> DNA

<213> modified NS4B

<400> 27

22137 Responses can only
be Artificial, Unknown
or Genus Species. See
Item 10 on Error Summary
Sheet.

RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 5, 24, 31, 392
Seq#:2; N Pos. 3, 9, 12, 15, 21, 24, 28, 30, 33, 71, 93, 1174
Seq#:3; Xaa Pos. 904, 1215
Seq#:4; N Pos. 3644

Use of <220> Feature(NEW RULES):

Sequence(s) are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence" or "Unknown". Please explain source of genetic material in <220> to <223> section (See "Federal Register," 6/01/98, Vol. 63, No. 104, pp.29631-32) (Sec.1.823 of new Rules)

Seq#:1, 2, 3, 4, 24

VERIFICATION SUMMARY DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893 TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

L:12 M:270 C: Current Application Number differs, Replaced Current Application No
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:27 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:31 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:35 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:39 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:43 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:44 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:46 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:16
L:92 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:384
L:128 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:132 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:136 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:140 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:144 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:148 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:152 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:156 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:160 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:164 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:168 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:172 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:176 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:177 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:178 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:60
L:196 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:1140
L:216 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:220 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:224 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:337 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:896
L:375 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:1200
L:411 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:415 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:419 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:480 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:3600
L:703 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:24
L:705 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:24, Line#:705